

**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION**
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): September 9, 2022

DAY ONE BIOPHARMACEUTICALS, INC.

(Exact name of registrant as specified in its charter)

Delaware
(State or other jurisdiction
of incorporation)

001-40431
(Commission
File Number)

83-2415215
(IRS Employer
Identification No.)

2000 Sierra Point Parkway, Suite 501
Brisbane, CA
(Address of principal executive offices)

94080
(Zip Code)

(650) 484-0899
(Registrant's telephone number, including area code)

N/A
(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

- Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
- Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
- Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
- Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, \$0.0001 Par Value Per Share	DAWN	The Nasdaq Stock Market LLC (Nasdaq Global Select Market)

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (17 CFR §230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (17 CFR §240.12b-2 of this chapter).

Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

Item 5.02 Departure of Directors or Certain Officers; Election of Directors; Appointment of Certain Officers; Compensatory Arrangements of Certain Officers.

Appointment of New Director

On September 9, 2022, upon the recommendation of the Nominating and Governance Committee (the “*Governance Committee*”) of the Board of Directors (the “*Board*”) of Day One Biopharmaceuticals, Inc. (the “*Company*”), the Board increased the size of the Board to nine directors and appointed Garry Nicholson as a Class 1 director, effective as of September 12, 2022 (the “*Effective Date*”). In connection with his appointment to the Board, Mr. Nicholson has been appointed as chairperson of the Board and as a member of the Governance Committee. Julie Papanek Grant, the prior chairperson of the Board, shall continue as a member of the Board.

In connection with his appointment as a non-employee director of the Board, and in accordance with the Company’s current compensation policy for non-employee directors (the “*Compensation Policy*”), the Board granted Mr. Nicholson a stock option to purchase shares of the Company’s common stock with an aggregate value of \$560,000, calculated in accordance with the Compensation Policy (the “*Initial Grant*”). The Initial Grant shall vest monthly over three years, beginning on the one-month anniversary of the Effective Date, subject, however, to Mr. Nicholson’s continued service on the Board on each vesting date.

Pursuant to the Compensation Policy, on the date of each annual meeting of the Company’s stockholders, each non-employee director who is serving on the Board prior to, and will continue to serve on the Board following, such meeting is entitled to an annual stock option grant for shares of the Company’s common stock with an aggregate value of \$280,000 (the “*Annual Grant*”), calculated in accordance with the Compensation Policy. Mr. Nicholson will be eligible for Annual Grants, provided, that, he satisfies the requirements set forth in the Compensation Policy, including the service requirements.

The Initial Grant and any Annual Grants awarded to Mr. Nicholson will be issued under the Company’s 2021 Equity Incentive Plan and will accelerate in full upon a change of control. Mr. Nicholson will also be entitled to the applicable annual cash retainer paid to non-employee directors under the Compensation Policy.

The Company has entered into its standard form of indemnification agreement with Mr. Nicholson. The form of the indemnification agreement was previously filed by the Company as Exhibit 10.1 to the Company’s registration statement on Form S-1 (File No. 333-255754) filed with the Securities and Exchange Commission on May 26, 2021 and incorporated by reference herein.

There are no arrangements or understandings between Mr. Nicholson and any other persons, pursuant to which Mr. Nicholson was selected as a member of the Board. There are also no family relationships among any of the Company’s other directors or executive officers and Mr. Nicholson. Mr. Nicholson does not have any other direct or indirect material interest in any transaction required to be disclosed pursuant to Item 404(a) of Regulation S-K.

Item 7.01 Regulation FD Disclosure.

On September 12, 2022, the Company issued a press release announcing the appointment disclosed above. A copy of this press release is attached hereto as Exhibit 99.1 and is incorporated by reference herein. Additionally, on September 12, 2022, the Company updated its corporate presentation. A copy of the updated corporate presentation is attached as Exhibit 99.2 and is also available on the Company’s website in the Events & Presentations section at www.dayonebio.com.

The information in this Item 7.01, including Exhibits 99.1 and 99.2 to this report, shall not be deemed to be “filed” for purposes of Section 18 of the Exchange Act, or otherwise subject to the liabilities of that section or Sections 11 and 12(a)(2) of the Securities Act. The information contained in this Item 7.01 and in the accompanying Exhibits 99.1 and 99.2 shall not be incorporated by reference into any other filing under the Exchange Act or under the Securities Act, except as shall be expressly set forth by specific reference in such filing.

Item 8.01 Regulation FD Disclosure.

On September 12, 2022, the Company updated guidance on the planned first patient dosing to the second half of 2022 for the Company's Phase 3 clinical trial (FIREFLY-2/LOGGIC) evaluating tovorafenib as a front-line therapy for patients newly diagnosed with pLGG.

Item 9.01 Financial Statement and Exhibits.

(d) Exhibits

Exhibit Number	Description
99.1	Press release issued by Day One Biopharmaceuticals, Inc. regarding the appointment of a new director dated September 12, 2022.
99.2	Corporate Presentation.
104	Cover Page Interactive Data File (embedded within the Inline XBRL document).

Forward-Looking Statements

This Current Report on Form 8-K contains forward-looking statements within the meaning of the U.S. Private Securities Litigation Reform Act of 1995 and other federal securities laws. Any statements contained herein that do not describe historical facts, including, but not limited to, statements we make regarding the timing of our Phase 3 clinical trial (FIREFLY-2/LOGGIC). Such risks and uncertainties include, among others, the risks identified in the Company's filings with the SEC, including its Quarterly Report on Form 10-Q for the quarter ended June 30, 2022, filed with the SEC on August 4, 2022, and other reports as filed with the SEC. The Company cautions you not to place undue reliance on any forward-looking statements, which speak only as of the date they are made. The Company undertakes no obligation to update publicly any forward-looking statements to reflect new information, events or circumstances after the date they were made or to reflect the occurrence of unanticipated events.

SIGNATURE

Pursuant to the requirements of the Securities Exchange Act of 1934, the Registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

DAY ONE BIOPHARMACEUTICALS, INC.

Date: September 12, 2022

By: /s/ Charles N. York II, M.B.A.

Name: Charles N. York II, M.B.A.

Title: Chief Operating Officer and Chief Financial Officer



Day One Appoints Garry Nicholson as Chairman of the Board of Directors

SOUTH SAN FRANCISCO, Calif., September 12, 2022 – Day One Biopharmaceuticals (Nasdaq: DAWN), a clinical-stage biopharmaceutical company dedicated to developing and commercializing targeted therapies for people of all ages with life-threatening diseases, today announced the appointment of Garry Nicholson as chairman of its board of directors. Mr. Nicholson brings more than 30 years of pharmaceutical and biotech oncology experience and previously served as president of Pfizer Oncology where he led its global oncology franchise. Day One co-founder Julie Grant, who served as board chair since 2021, will continue to serve as a member of the board of directors.

“Garry is an accomplished leader in the development and commercialization of new cancer therapies and we are thrilled to welcome him as chairman of our board of directors,” said Jeremy Bender, Ph.D., chief executive officer of Day One. “Garry’s expertise and guidance will be critical as tovorafenib continues to advance in our pivotal FIREFLY-1 trial towards potential commercialization for relapsed pediatric low-grade glioma and as our other ongoing clinical trials continue to progress.”

Mr. Nicholson currently serves as chairman of the board of directors for G1 Therapeutics and as a board member for Tmunity Therapeutics and NextCure. He also previously served on the board of directors for Turning Point Therapeutics, Five Prime Therapeutics and TESARO prior to their acquisitions by large pharmaceutical companies. As former president of Pfizer Oncology, his responsibilities included global commercialization, sales, clinical development, regulatory strategy and business development for Pfizer’s oncology portfolio. Earlier in his career, Mr. Nicholson held various leadership positions in the oncology division of Eli Lilly and Company, including global oncology platform leader. He has also served as president and CEO of XTuit Pharmaceuticals. Mr. Nicholson earned a B.S. in Pharmacy from the University of North Carolina at Chapel Hill and an M.B.A. from the University of South Carolina.

“Day One is an innovative company dedicated to advancing new cancer therapies for people of all ages and I could not be more excited to join its board of directors as chairman,” said Mr. Nicholson. “Tovorafenib has the potential to become a meaningful new targeted treatment for pediatric low-grade glioma, a devastating form of childhood brain cancer, and I look forward to applying my oncology market experience as the company prepares for potential commercialization.”

About Tovorafenib

Tovorafenib is an investigational, oral, brain-penetrant, highly selective type II pan-RAF kinase inhibitor designed to target a key enzyme in the MAPK signaling pathway, which is being investigated in primary brain tumors and solid tumors harboring activating RAF alterations. Tovorafenib has been studied in over 325 patients to date. Currently tovorafenib is under evaluation in a pivotal Phase 2 clinical trial (FIREFLY-1) among pediatric, adolescent and young adult patients with relapsed pediatric low-grade glioma (pLGG), which is an area of considerable unmet need with no approved therapies for the majority

of patients. Day One has also initiated a pivotal Phase 3 study (FIREFLY-2/LOGGIC) in newly-diagnosed patients with pLGG. Beyond pLGG, tovorafenib is being evaluated alone or as a combination therapy for adolescent and adult patient populations with recurrent or progressive solid tumors with MAPK pathway aberrations (FIRELIGHT-1). Tovorafenib has been granted Breakthrough Therapy and Rare Pediatric Disease designations by the U.S. Food and Drug Administration (FDA) for the treatment of patients with pLGG harboring an activating RAF alteration. Tovorafenib has also received Orphan Drug designation from the FDA for the treatment of malignant glioma, and from the European Commission (EC) for the treatment of glioma.

About Day One Biopharmaceuticals

Day One Biopharmaceuticals is a clinical-stage biopharmaceutical company that believes when it comes to pediatric cancer, we can do better. We put kids first and are developing targeted therapies that deliver to their needs. Day One was founded to address a critical unmet need: the dire lack of therapeutic development in pediatric cancer. The Company's name was inspired by the "The Day One Talk" that physicians have with patients and their families about an initial cancer diagnosis and treatment plan. Day One aims to re-envision cancer drug development and redefine what's possible for all people living with cancer—regardless of age—starting from Day One.

Day One partners with leading clinical oncologists, families, and scientists to identify, acquire, and develop important emerging cancer treatments. The Company's lead product candidate, tovorafenib (DAY101), is an investigational, oral, brain-penetrant, highly-selective type II pan-RAF kinase inhibitor. The Company's pipeline also includes pimasertib, an investigational, oral, highly-selective small molecule inhibitor of mitogen-activated protein kinases 1 and 2 (MEK-1/-2). Day One is based in South San Francisco. For more information, please visit www.dayonebio.com or find the company on LinkedIn or Twitter.

Cautionary Note Regarding Forward-Looking Statements

This press release contains "forward-looking" statements within the meaning of the "safe harbor" provisions of the Private Securities Litigation Reform Act of 1995, including, but not limited to: Day One's plans to develop cancer therapies, expectations from current clinical trials, the execution of the Phase 2 and Phase 3 clinical trial for tovorafenib (DAY101) as designed, any expectations about safety, efficacy, timing and ability to complete clinical trials, release data results and to obtain regulatory approvals for tovorafenib (DAY101) and other candidates in development, and the ability of tovorafenib (DAY101) to treat pLGG or related indications.

Statements including words such as "believe," "plan," "continue," "expect," "will," "develop," "signal," "potential," or "ongoing" and statements in the future tense are forward-looking statements. These forward-looking statements involve risks and uncertainties, as well as assumptions, which, if they do not fully materialize or prove incorrect, could cause our results to differ materially from those expressed or implied by such forward-looking statements.

Forward-looking statements are subject to risks and uncertainties that may cause Day One's actual activities or results to differ significantly from those expressed in any forward-looking statement, including risks and uncertainties in this press release and other risks set forth in our filings with the Securities and Exchange Commission, including Day One's ability to develop, obtain regulatory approval for or commercialize any product candidate, Day One's ability to protect intellectual property, the potential impact of the COVID-19 pandemic and the sufficiency of Day One's cash, cash equivalents and investments to fund its operations. These forward-looking statements speak only as of the date hereof and Day One specifically disclaims any obligation to update these forward-looking statements or reasons why actual results might differ, whether as a result of new information, future events or otherwise, except as required by law.

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Targeted Therapies for People of All Ages

September 2022

Disclaimer

This presentation and the accompanying oral commentary contain forward-looking statements that are based on our management's beliefs and assumptions and on information currently available to our management. Forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified. In some cases, you can identify forward-looking statements by terminology such as "may," "will," "should," "could," "expect," "plan," "anticipate," "believe," "estimate," "predict," "intend," "potential," "would," "continue," "ongoing" or the negative of these terms or other comparable terminology. Forward-looking statements include all statements other than statements of historical fact contained in this presentation, including information concerning our future financial performance, including the sufficiency of our cash and cash equivalents to fund our operations, business plans and objectives, timing and success of our planned nonclinical and clinical development activities, timing and results of nonclinical studies and clinical trials, efficacy and safety profile of our product candidates, the execution of the Phase 2 clinical trial for DAY101 and the Phase 1b/2 clinical trial for DAY101 and pimasetrib as designed, any expectations about safety, efficacy, timing and ability to complete clinical trials and to obtain regulatory approvals for DAY101 and other candidates in development, the ability of DAY101 to treat pLGG or related indications, the potential therapeutic benefits and economic value of our product candidates, potential growth opportunities, competitive position, industry environment and potential market opportunities, our ability to protect intellectual property, and the impact of the COVID-19 pandemic on our business and operations.

Forward-looking statements are subject to known and unknown risks, uncertainties, assumptions and other factors. It is not possible for our management to predict all risks, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements we may make. These factors, together with those that are described under the heading "Risk Factors" contained in our most recent Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission ("SEC") and other documents we file from time to time with the SEC, may cause our actual results, performance or achievements to differ materially and adversely from those anticipated or implied by our forward-looking statements.

In addition, statements that "we believe" and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this presentation, and although we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted a thorough inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain and investors are cautioned not to unduly rely upon these statements. Furthermore, if our forward-looking statements prove to be inaccurate, the inaccuracy may be material. In light of the significant uncertainties in these forward-looking statements, you should not regard these statements as a representation or warranty by us or any other person that we will achieve our objectives and plans in any specified time frame, or at all. We undertake no obligation to publicly update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

This presentation also contains estimates and other statistical data made by independent parties and by us relating to market size and growth and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. In addition, projections, assumptions, and estimates of our future performance and the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk.

Day One: Developing Targeted Therapies That Address The Urgent Needs of Children With Cancer

Mission That Creates Value

- Day One's mission is to help children with cancer, from day one and every day after
- Develop medicines for genomically-defined cancers
- Establish first-in-class position through rapid pediatric registration
- Expand to adolescent and adult populations in parallel and pursue those opportunities with the same commitment we do for children

Tovorafenib (DAY101) Lead Program

- Investigational, oral, CNS-penetrant pan-RAF inhibitor
- Being studied as tablets and pediatric-friendly liquid suspension
- Breakthrough Therapy Designation
- Rare Pediatric Disease Designation
- Orphan Drug Designation (US/EU)

Growing Portfolio and Runway Beyond Clinical Milestones

- Two clinical-stage MEKi assets, in-licensed for combination trials
- Projected cash runway into 2025
- Multiple key milestones
 - Top-line data from FIREFLY-1 trial in Q1 2023
 - NDA submission in 1H 2023, if data are supportive
 - First patient dosing in pivotal Phase 3 (FIREFLY-2 /LOGGIC), frontline trial expected 2H 2022

Pediatric Markets Create Opportunity for High Impact and Capital Efficiency



Regulatory and reimbursement tailwinds

- Lack of approved products create potential first-in-class opportunities
- Pricing flexibility for important new therapies
- Supportive and engaged advocacy and investigator community desiring better treatment options



Rapid clinical development

- Early engagement with global regulatory authorities
- Small trials and clear endpoints that permit rapid development to clinical proof-of-concept and potential approval



Enriched responder populations informed by underlying biology

- Many pediatric tumors are genetically simple and genomically stable
- Genetic alterations are often oncogenic

A Senior Team with Deep Experience Developing and Commercializing Products in Pediatric and Adult Oncology Markets



Jeremy Bender, PhD, MBA
Chief Executive Officer

VP of Corporate Development at Gilead; COO Tizona Therapeutics; CBO Sutro Biopharma; founding Board member of VaxCytte



Samuel Blackman, MD, PhD
Chief Medical Officer & Founder

Pediatric Heme/Onc and Neuro-Onc; Oncology Clinical Development at Mavupharma, Silverback, Juno, Seattle Genetics, GSK



Charles York II, MBA
Chief Operating and Financial Officer

CFO and Head of Corporate Development at Aeglea; Consulting CFO at Bridgepoint Consulting; PricewaterhouseCoopers



Mike Preigh, PhD
Chief Technical Officer

Head of CMC at Array for 10+ years. Brought >20 drug candidates to IND & clinical development



Davy Chiodin, PharmD
Chief Development Officer



VP Regulatory Science, Acerta/AZ; Global Regulatory Leader, Pediatric Oncology, Roche/Genentech



Jaa Roberson
Chief People Officer

Head of Human Resources at Bellicum Pharmaceuticals; Human Resources Roles at Achaogen, Roche/Genentech

Our Pipeline

Product Candidate	Indication	Preclinical	Phase 1	Phase 2	Phase 3	Recent & Anticipated Milestones
Tovorafenib (DAY101) Type II Pan-RAF Inhibitor ✓ FDA Breakthrough Therapy Designation for relapsed pLGG ✓ FDA Rare Pediatric Disease Designation (PRV Eligible) for pLGG ✓ FDA Orphan Drug Designation for gliomas ✓ EC Orphan Designation for gliomas	Relapsed pLGG	FIREFLY-1 ¹ (pivotal) 				Pivotal cohort enrollment complete: May 2022 Initial data presented: June 2022 Topline data expected: Q1 2023
	Frontline pLGG	FIREFLY-2 (pivotal) 				Trial Initiation: June 2022 First patient dosing expected: 2H 2022
	RAF-altered solid tumors ² (monotherapy)	FIRELIGHT-1* 				First patient dosed: November 2021
Pimasertib MEK 1/2 Inhibitor	MAPK-altered solid tumors ³ (Combo w/tovorafenib)	FIRELIGHT-1* 				First patient dosed: May 2022

*Includes patients ≥12 years of age. ¹ FIREFLY-1 Arm 1 expected to support registration. ² DAY101 adult monotherapy Phase 1 dose escalation and expansion trial previously completed. ³ Pimasertib Phase 1 dose escalation and expansion trial previously completed. pLGG, pediatric low-grade glioma. Tovorafenib and Pimasertib are investigational products. Safety and efficacy have not been established by any health authority.
 Day One Biopharmaceuticals

Tovorafenib (DAY101)

Type II Pan-RAF Inhibitor

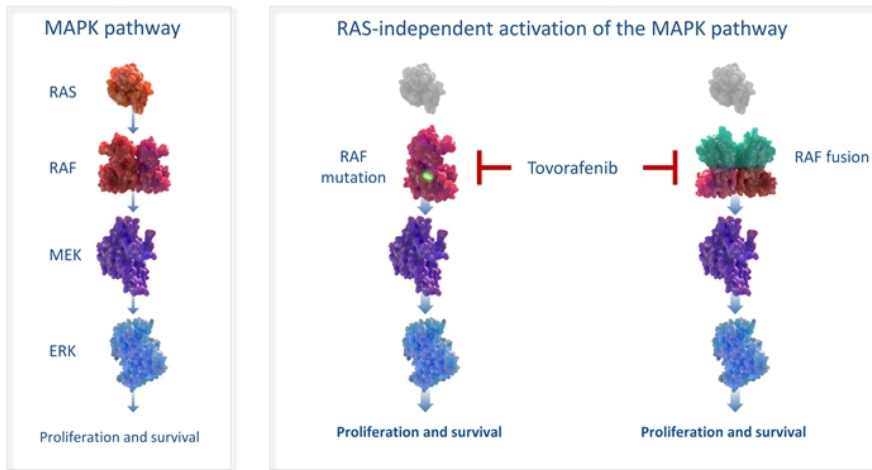
Pediatric Low-Grade Gliomas (pLGG)



6 y/o with large relapsed BRAF fusion-positive optic pathway glioma

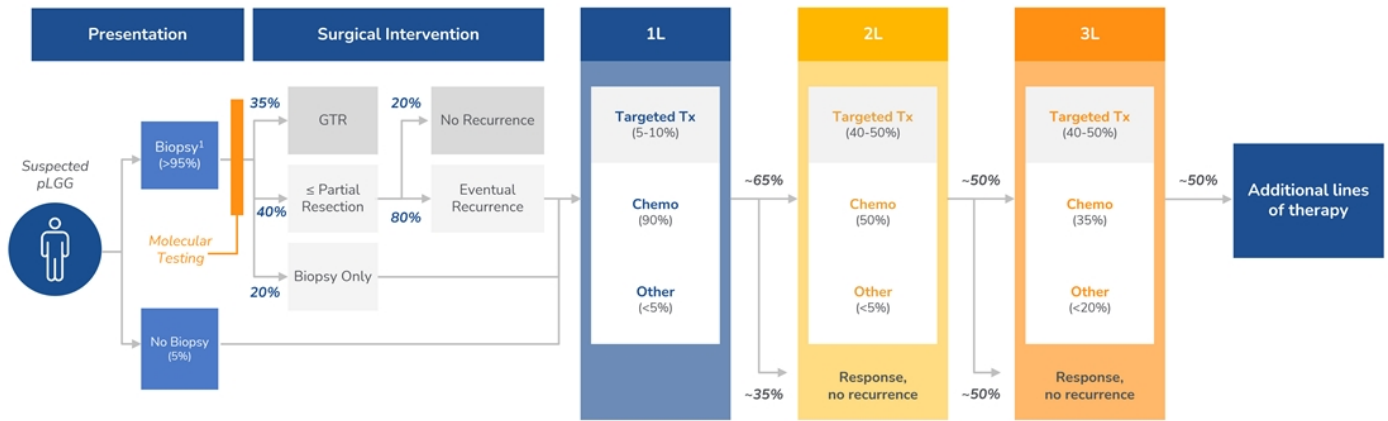
- Despite being the most common brain tumor in children, there are no approved agents and no standard-of-care for the majority of patients with relapsed/progressive disease^{1,2}
 - 70% of patients will require systemic therapy
 - Patients have a high rate of recurrence and are frequently treated with multiple lines of systemic therapy over the course of their disease
- The majority of pLGGs are driven by BRAF alterations³
 - 85% of BRAF-altered tumors harbor a *KIAA1549-BRAF* gene fusion
 - 15% are driven by BRAF V600E mutation
- Despite low-grade histology and high long-term survival, pLGGs are chronic and relentless¹⁻⁴
 - Goal of therapy is to stabilize or shrink tumors while minimizing treatment-associated toxicities from surgery, chemotherapy, and radiation
 - Many patients today suffer profound tumor and treatment-associated morbidity and significant late effects that persist throughout life

Tovorafenib (DAY101) Inhibits Both BRAF Fusions and BRAF V600 Mutations



- **Tovorafenib (DAY101) is an investigational, oral, selective, CNS-penetrant, type II pan-RAF inhibitor that was designed to inhibit both monomeric and dimeric RAF kinase**
 - Activity in tumors driven by both RAF wild-type fusions and BRAF V600E mutations
 - Tablet and pediatric-friendly liquid suspension; once weekly dosing
- **Currently approved type I RAFi are indicated for use only in adults and patients 6+ with relapsed tumors harboring a BRAF V600 mutation**
 - Type I RAF inhibitors cause paradoxical MAPK activation in the setting of wild-type RAF, increasing the risk of tumor growth in BRAF fusion-driven and other non-V600 mutant cancers

The Current pLGG Treatment Paradigm Reflects the Unrelenting Nature of this Chronic Brain Tumor



Because many pLGGs undergo senescence when patients reach their 20s, the goal of therapy is to **maximize tumor control** while **minimizing treatment-associated toxicities** from surgery, chemotherapy, and radiation. As a result, a large number of pLGG patients will undergo **multiple lines of systemic therapy** over the course of their disease.

Source: Physician Interviews, Bandopadhyay et al. *Pediatric Blood Cancer*, 2014; Sievert and Fischer. *J Child Neurol*, 2009; ClearView Analysis. GTR: Gross Total Resection 1Molecular testing of biopsied samples occurs in all patients. Kandels et al. *Retrospective analysis of comprehensive SIOP registry*; Hargrave et al. *Phase I/II*; Fangusaro et al. *Phase II*

Pivotal Phase 2 Trial Of Monotherapy Tovorafenib (DAY101) In Relapsed Or Progressive pLGG (FIREFLY-1)

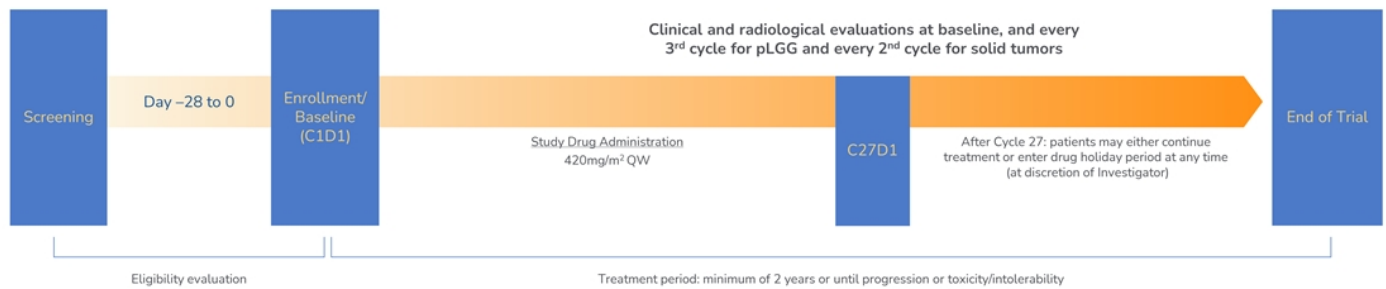


Trial Design

- Three arm, open-label, global registrational phase 2 trial
- Pivotal Arm 1 (recurrent/progressive LGG): n = ~ 60 RANO-evaluable patients aged 6 months to 25 years harboring a KIAA1549-BRAF fusion or BRAF V600 mutation
- Arm 2 (expanded access recurrent/progressive LGG): patients aged 6 months to 25 years harboring an activating RAF alteration
- Arm 3 (extracranial solid tumors): patients aged 6 months to 25 years harboring an activating RAF fusion

Endpoints (Pivotal Arm 1)

- Primary endpoint: ORR based on RANO criteria, assessed by blinded independent central review
- Secondary endpoints: ORR by RAPNO criteria; PFS; safety

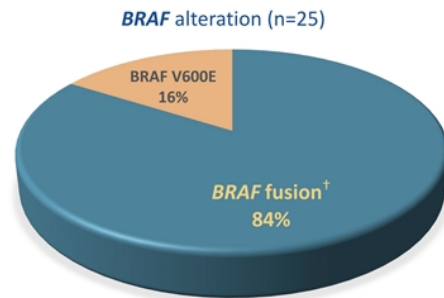
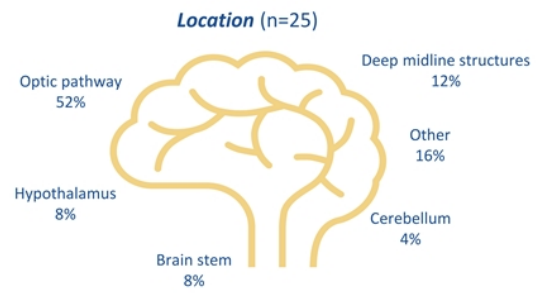


Abbreviations: C, cycle; D, day; LGG, low-grade glioma; ORR, objective response rate; PFS, progression-free survival.
NCT04775485

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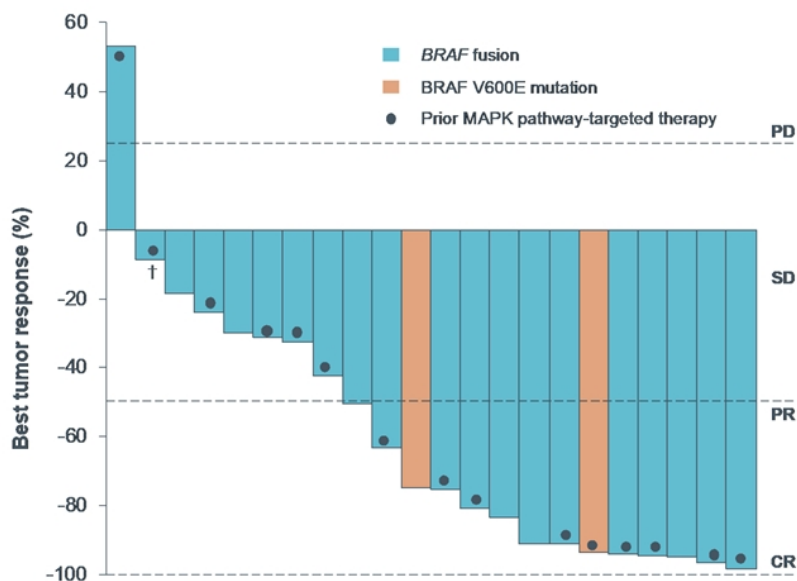
Baseline Characteristics

Characteristic	Arm 1 (N=25)
Median age, years (range)	8 (3-18)
Sex, n (%)	
Male	13 (52)
Female	12 (48)
Race, n (%)	
Black or African American	1 (4)
Asian	2 (8)
White	15 (60)
Other*	7 (28)
Karnofsky/Lansky performance status, n (%)	
50-70	1 (4)
80-100	24 (96)
Number of lines of prior therapy	
Median (range)	3 (1-9)
1, n (%)	5 (20)
2, n (%)	6 (24)
≥3, n (%)	14 (56)
Prior MAPK pathway targeted therapy, n (%)	
Yes	18 (72)
No	7 (28)



Apr 14, 2022 data cutoff; *Includes 4 patients with race not specified. [†]Includes 2 patients with BR*A*F duplication and 1 with BR*A*F rearrangement per fluorescence in situ hybridization. MAPK, mitogen-activated protein kinase; prior MAPK pathway targeted therapy indicates either prior MEK*i* and/or prior type I RAF*i* therapy.

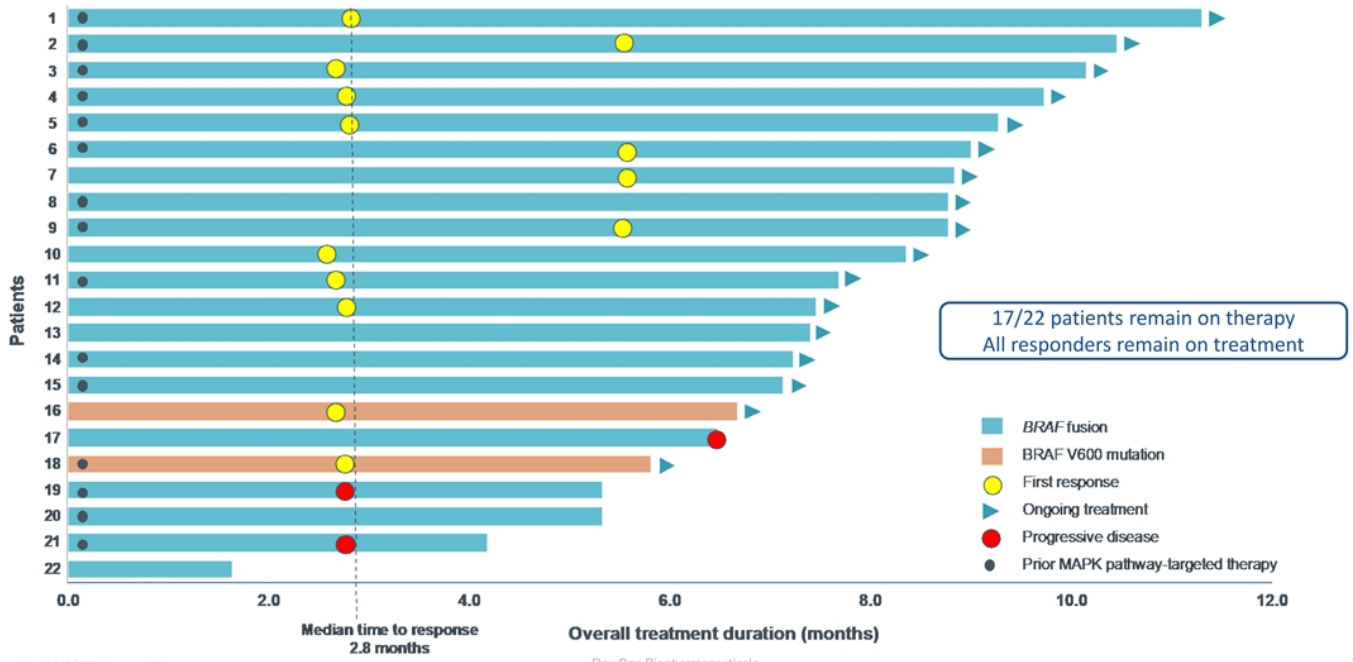
Tumor Response To Tovorafenib (DAY101) For All Patients With RANO-Evaluable Lesions (n=22)*



Response (IRC)	RANO Evaluable N=22*
ORR (95% CI)	64% (41-83)
BRAF fusion (n=20)	60%
BRAF V600E (n=2)	100%
CBR#	91%
Best overall response	
PR (13/22)	59%
uPR (1/22)	5%
SD (6/22)	27%

Apr 14, 2022 data cutoff. Total % of response maybe may be different than the sum of the individual overall response due to rounding. *3/25 patients lacked evaluable lesions per RANO criteria based on IRC evaluation. †Progressive disease due to presence of new lesions. #patients with best overall response of CR, PR/uPR and SD. CBR, clinical benefit rate; IRC, independent radiological review committee; ORR, overall response rate; MAPK, mitogen-activated protein kinase; PR, partial response; SD, stable disease; uPR, unconfirmed partial response

Duration of Tovorafenib (DAY101) Therapy For All Patients with RANO-Evaluable Lesions (n=22)

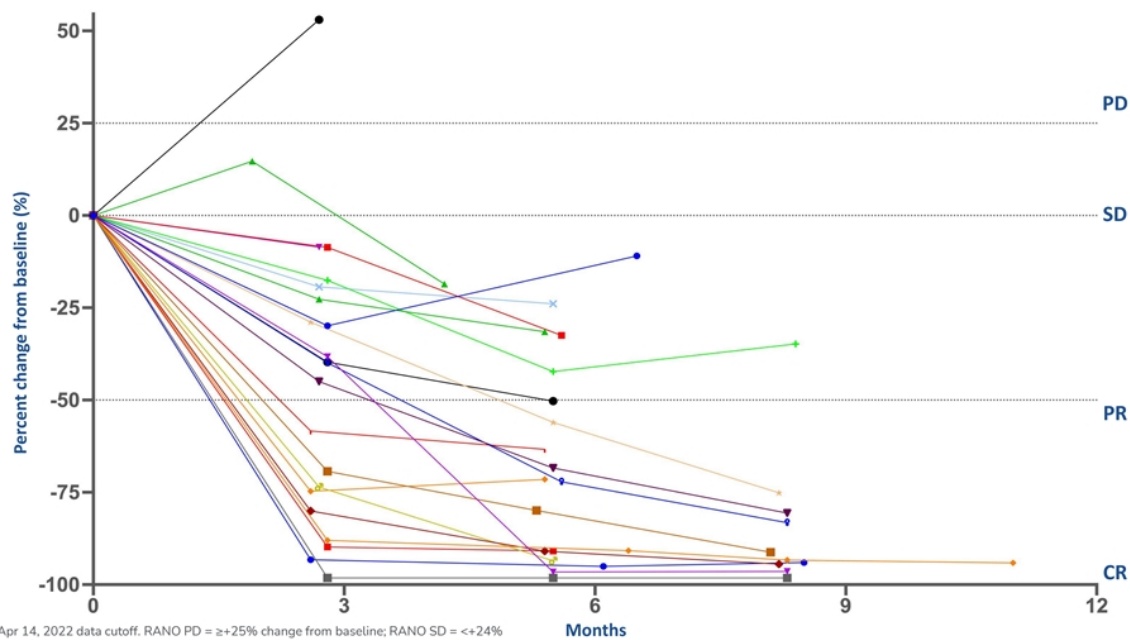


Apr 14, 2022 data cutoff.

Day One Biopharmaceuticals

Individual Patient Tumor Change From Baseline

(n=22 RANO-Evaluable By Blinded Independent Central Review)



Tovorafenib (DAY101) Safety Data For the First 25 Enrolled Patients (TEAEs ≥25% Any Grade)

Preferred term, n (%)	Treatment-emergent AEs		Treatment-related AEs	
	Any grade	Grade ≥3	Any grade	Grade ≥3
Blood creatine phosphokinase increased	20 (80)	2 (8)	18 (72)	2 (8)
Hair color changes	17 (68)	-	17 (68)	-
Anemia	14 (56)	3 (12)	10 (40)	2 (8)
Aspartate aminotransferase increased	14 (56)	-	12 (48)	-
Vomiting	14 (56)	2 (8)	6 (24)	1 (4)
Rash*	13 (52)	3 (12)	13 (52)	3 (12)
Blood lactate dehydrogenase increased	12 (48)	-	9 (36)	-
Headache	10 (40)	-	3 (12)	-
Dry skin	9 (36)	-	7 (28)	-
Epistaxis	9 (36)	-	4 (16)	-
Constipation	8 (32)	-	5 (20)	-
Hypocalcemia	8 (32)	-	6 (24)	-
Nausea	8 (32)	-	3 (12)	-
Alanine aminotransferase increased	7 (28)	1 (4)	4 (16)	1 (4)
Fatigue	7 (28)	-	7 (28)	-

- Most treatment-emergent AEs were grade 1 or 2 (96%)
- Other important treatment-emergent AEs included:
 - Decreased weight (24%)
 - Decreased appetite (16%)
 - Hyponatremia (16%)
- 7 patients (28%) required dose modifications due to treatment-related AEs
- No patient discontinued treatment due to AEs

Apr 14, 2022 data cutoff. AE, adverse event. TEAE, treatment-emergent adverse event.
*Includes maculopapular and erythematous rash

Key Takeaways

- **Encouraging initial efficacy data from FIREFLY-1 for pediatric patients with relapsed LGG harboring BRAF fusion or BRAF V600 mutation, for whom there is no standard-of-care and no approved agents for the majority of patients**
 - 64% ORR and 91% clinical benefit rate (partial response/unconfirmed partial response + stable disease) in the 22 RANO-evaluable patients:
 - 14 partial responses (13 confirmed responses and 1 unconfirmed response)
 - 6 patients with stable disease
 - All patients with stable disease (n=6) were noted to have tumor shrinkage, ranging between 19% and 43%
 - Responses were observed in patients with both BRAF fusions and BRAF V600E mutations who received prior MAPK-targeted therapy
 - The median-time-to-response was 2.8 months
 - A heavily-pretreated population, with a median of 3 prior lines of therapy (range: 1-9)
 - All patients who responded remain on therapy (n=14) and no patients have discontinued treatment due to treatment-related adverse events
- **Initial safety data, based on the first 25 patients, indicated monotherapy tovorafenib (DAY101) to be generally well-tolerated**
 - Majority of AEs were grade 1 or 2; most common treatment-related AEs were CPK elevation, rash, and hair color changes
 - Treatment-related AEs of grade 3 or greater occurred in nine patients (36%)
- **Plan to present additional initial study results from FIREFLY-1 at an upcoming medical conference in 2H 2022**
- **Topline results from the full registrational cohort (n=~60) of FIREFLY-1 expected to be available 1Q 2023, with NDA submission planned for 1H 2023**
- **Early results from FIREFLY-1 support plan to evaluate tovorafenib (DAY101) in parallel with a pivotal Phase 3 frontline pLGG study (FIREFLY-2)**
 - Primary endpoint of ORR based on RANO criteria, assessed by blinded independent central review

Incidence and Prevalence of BRAF-altered pLGG in the U.S.

	2020 Estimated Incidence Under 25	2017 Estimated SEER Prevalence Under 25
US Population ¹	~105,000,000	NA
Rate of CNS Tumors (0.00521%) ²	~5,500	~130,000 ³
Gliomas (63%) ²	~3,500	~82,000
Low Grade (77%) ²	~2,600	~63,000
Has Received Drug Tx (58%) ²	~1,500	~36,000
BRAF Mutated (70%) ²	~1,100	~26,000
	~1,100 Estimated Annual Incidence	~26,000 Estimated Prevalence (SEER)

¹ US Census; ² CBTRUS, Qaddoumi et al 2009, Schreck et al 2019, ClearView Analysis; ³ SEER US complete prevalence counts of patients aged under 25 with Brain and Other Nervous Systems tumors as of January 1, 2017.

Estimated annual incidence and estimated prevalence (SEER) are Day One calculations based on publicly available data.

FIREFLY-2/LOGGIC

Pivotal Phase 3 Trial of Tovorafenib (DAY101) in
Newly Diagnosed pLGG

FIREFLY-2/LOGGIC Pivotal Phase 3 Trial Of Tovorafenib (DAY101) In Newly Diagnosed pLGG

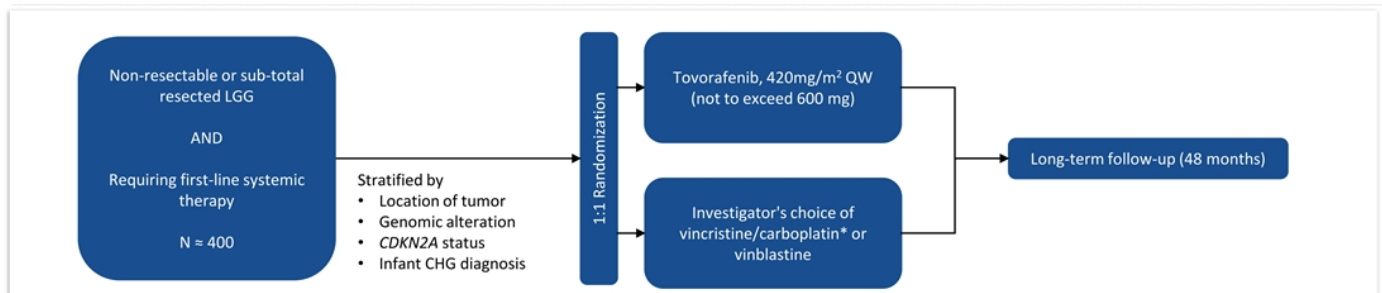


Trial Design

- Randomized, global, registrational Phase 3 trial of monotherapy tovorafenib (DAY101) vs SoC chemotherapy
- Eligibility: Patients aged 6 months to <25 years with LGG harboring a RAF alteration and requiring first-line systemic therapy
- Tovorafenib (DAY101) available as tablets and pediatric-friendly liquid suspension
- Patients who progress after stopping tovorafenib (DAY101) may be re-challenged
- Patients who progress in the SoC arm during or post-treatment may cross-over to receive tovorafenib

Endpoints

- **Primary endpoint:** ORR based on RANO criteria, assessed by blinded independent central review
- Key secondary endpoints: PFS and DoR by RANO criteria, ORR by RAPNO criteria
- Other secondary endpoints: changes in neurological and visual function, safety, and tolerability
- Key exploratory objectives: QoL and health utilization measures



* COG or SIOPe-LGG regimen
Abbreviations: CHG, chiasmatic, hypothalamic glioma; DoR, duration of response; LGG, low-grade glioma; ORR, objective response rate; QoL, quality of life; QW, once weekly; SoC, standard of care

Day One Biopharmaceuticals

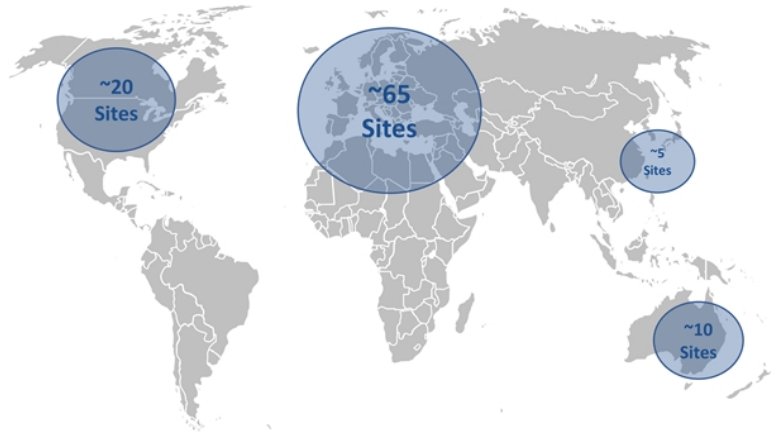
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FIREFLY-2/LOGGIC: Pivotal Phase 3 Study Of Tovorafenib (DAY101) In Newly Diagnosed pLGG

- **Collaboration between Day One and the LOGGIC consortium, internationally recognized experts in pLGG research**
 - Coupled with the LOGGIC-CORE molecular diagnostic program
 - Worked jointly on the study design and discussions with the U.S. and EU regulatory authorities
- **Approximately 100 potential sites (~65 from the LOGGIC consortium)**





LOGGIC
EUROPE

LOGGIC: Low Grade Glioma In Children



Day One Biopharmaceuticals

Our Pipeline

Product Candidate	Indication	Preclinical	Phase 1	Phase 2	Phase 3	Recent & Anticipated Milestones
Tovorafenib (DAY101) Type II Pan-RAF Inhibitor ✓ FDA Breakthrough Therapy Designation for relapsed pLGG ✓ FDA Rare Pediatric Disease Designation (PRV Eligible) for pLGG ✓ FDA Orphan Drug Designation for gliomas ✓ EC Orphan Designation for gliomas	Relapsed pLGG	FIREFLY-1 ¹ (pivotal) 				Pivotal cohort enrollment complete: May 2022 Initial data presented: June 2022 Topline data expected: Q1 2023
	Frontline pLGG	FIREFLY-2 (pivotal) 				Trial Initiation: June 2022 First patient dosing expected: 2H 2022
	RAF-altered solid tumors ² (monotherapy)	FIRELIGHT-1* 				First patient dosed: November 2021
Pimasertib MEK 1/2 Inhibitor	MAPK-altered solid tumors ³ (Combo w/tovorafenib)	FIRELIGHT-1* 				First patient dosed: May 2022

*Includes patients ≥12 years of age. ¹ FIREFLY-1 Arm 1 expected to support registration. ² DAY101 adult monotherapy Phase 1 dose escalation and expansion trial previously completed. ³ Pimasertib Phase 1 dose escalation and expansion trial previously completed. pLGG, pediatric low-grade glioma. Tovorafenib and Pimasertib are investigational products. Safety and efficacy have not been established by any health authority.
 Day One Biopharmaceuticals

Tovorafenib (DAY101) is Active as a Monotherapy in Patients with RAF-altered Adult Solid Tumors and Has Shown Strong Synergy Preclinically in Combination



Clinical activity demonstrated in relapsed melanoma patients; preclinical activity demonstrated in RAF fusions, BRAF non-V600 mutations, and BRAF V600 mutations

- >225 adult patient exposures
- Responses in BRAF V600E mutant tumors similar to type I BRAF inhibitors
- Responses in relapsed BRAF and NRAS-mutant melanoma, suggesting tovorafenib (DAY101) may be active in tumors currently unaddressed by approved Type I BRAF inhibitors



Differentiated safety profile for tovorafenib (DAY101) vs. existing BRAF and MEK inhibitors

- Less frequent and less severe acneiform rash
- No observed ophthalmologic liabilities (RVO/CSR)
- No observed CV liabilities (changes in LVEF)
- No type I BRAF SAEs: SCCs/KAs, pyrexia, arthralgia



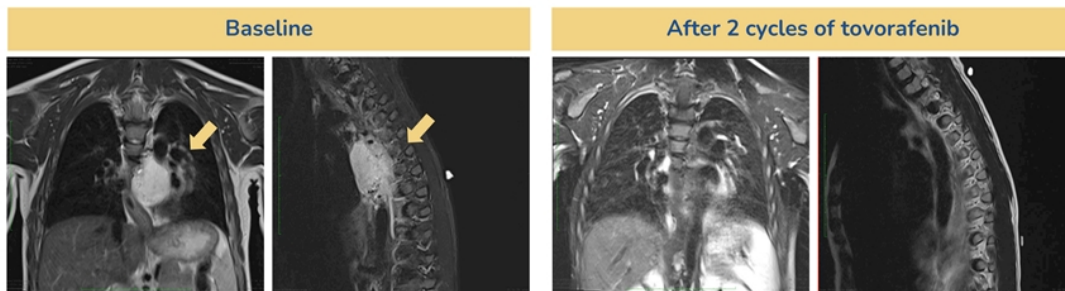
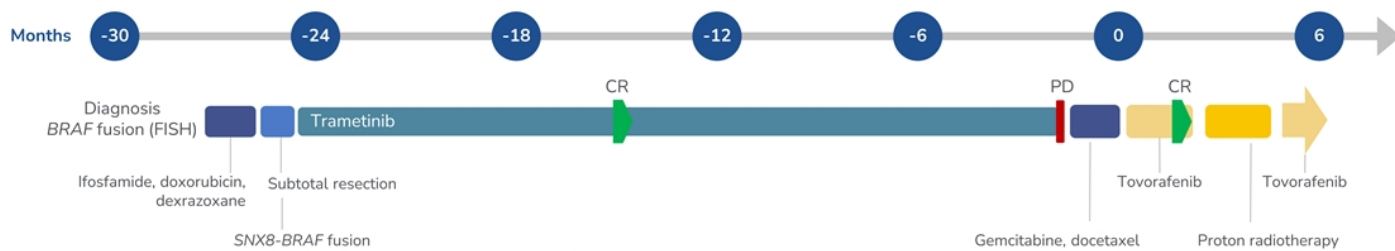
We **initiated** an adult solid tumor **study** to further evaluate monotherapy tovorafenib (DAY101) in patients with RAF altered tumors for which there are no currently approved therapies

- Same study will include combination cohorts of tovorafenib (DAY101) + pimasertib
- First patient dosed in Phase 2 monotherapy study in November 2021

Source: Olszanski AJ et. al. European Society for Medical Oncology Congress; Poster #410P, 2017
Unpublished clinical study results

Activity of Tovorafenib (DAY101) in SNX8:BRF Fusion Spindle Cell Sarcoma

A male child spindle cell sarcoma, 5-years of age at diagnosis

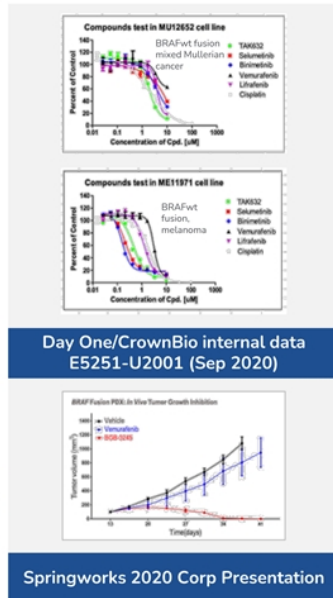
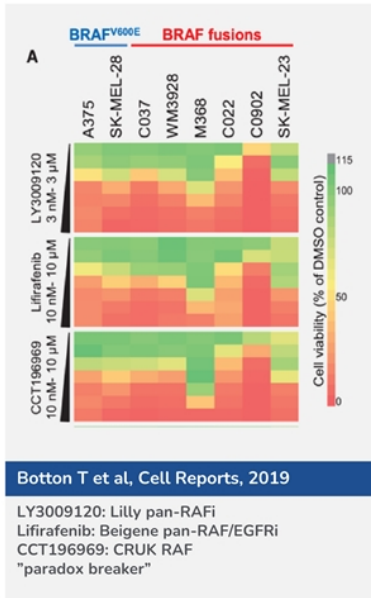


- After the first dose of tovorafenib (DAY101), the patient experienced grade 2 rash, which resolved in a day following a dose of diphenhydramine
- Radiotherapy-related adverse events included hyperpigmentation overlying the spine on the upper back with no skin breaks, and mild dysphagia

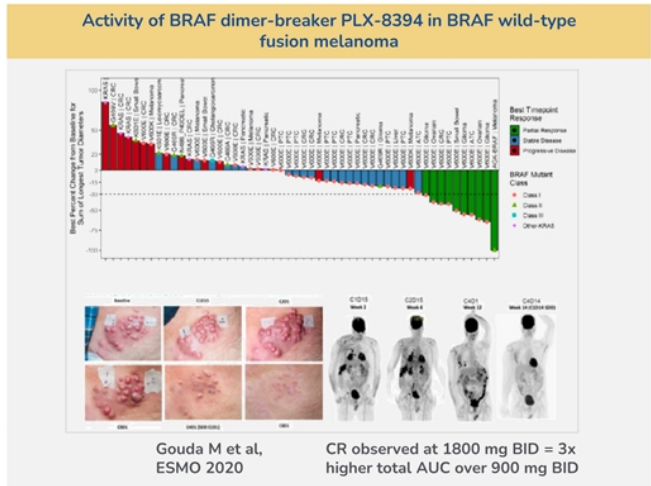
Data cut off: September 30, 2021

Day One Biopharmaceuticals

Next-generation RAF Inhibitors are Unique in Their Ability to Address Adult Cancers Associated with RAF Wild-type Fusions



Only tovorafenib (DAY101) has demonstrated *monotherapy clinical activity* in KIAA1549:BRAF and SRGAP3:CRAF wild-type fusions in pLGG



Phase 2 Study of Monotherapy Tovorafenib (DAY101) in Solid Tumors (FIRELIGHT-1)

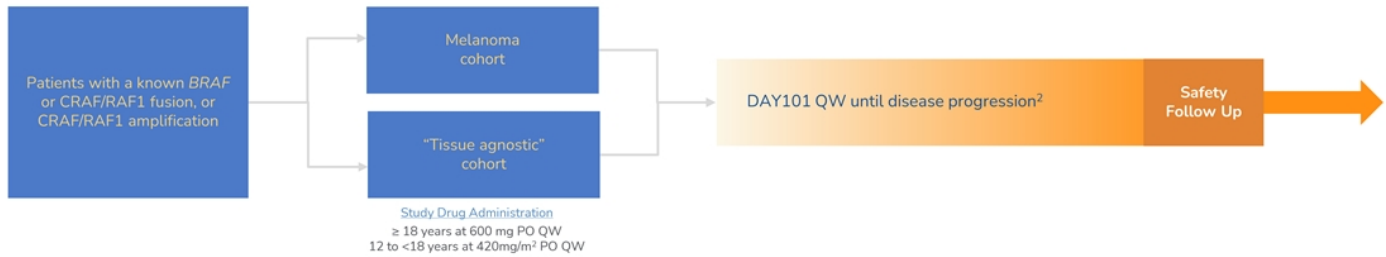


Trial Design¹

- Single arm, open-label, global phase 1b/2a trial
- n = 40 patients (approximately)
- Eligibility: Patients aged 12 years and older with non-hematologic tumor with an activating BRAF fusion, CRAF/RAF1 fusion, or CRAF/RAF1 amplification

Endpoints

- Primary endpoint: ORR by RECIST version 1.1 for non-CNS solid tumors and RANO criteria for any CNS tumors
- Secondary endpoints: safety and additional efficacy parameters







Abbreviations: ORR, objective response rate; QW, once weekly; PO, by mouth; BRAF, B-Raf proto-oncogene.⁰

1. Umbrella master study – DAY101-102 (main protocol) DAY101 and MAPK pathway aberration, Sub-study 1 monotherapy (DAY101-102a), Sub-study 2 MEK combo (DAY101-102b).

2. DAY101 QW until disease progression, intolerable toxicity, withdrawal of consent, or death

Strong Scientific Rationale for Combining Tovorafenib (DAY101) with Additional MAPK Pathway Inhibitors

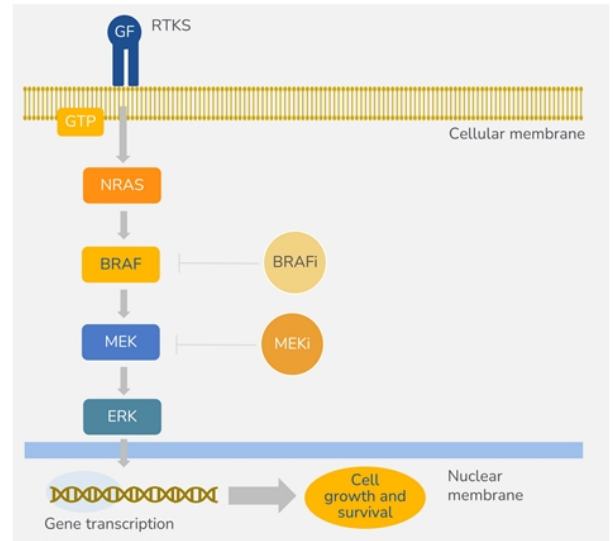
	BRAF non-V600	BRAF or CRAF WT fusion	KRAS or NRAS mutant	NF1 LOF
Signaling pathways	 <p>Proliferation, survival</p>	 <p>Proliferation, survival</p>	 <p>Proliferation, survival</p>	 <p>Proliferation, survival</p>
Potential combinations	Type II RAFi + MEKi or SHP2i	Type II RAFi + MEKi	Type II RAFi + KRAS - G12Ci or MEKi or SHP2i	Type II RAFi + SHP2i
Rationale	Non V600 BRAF dimers are effectively inhibited by type II, but not type I, RAFi	BRAF fusion dimers are effectively inhibited by type II, but not type I RAFi	Targeting multiple nodes of MAPK pathway will drive deeper and more durable response	Targeting multiple pathways will drive deeper response

Pimasertib

MEK1/2 Inhibitor

Pimasertib: Allosteric MEK1/2 Inhibitor with Demonstrated Activity in MAPK-driven Solid Tumors

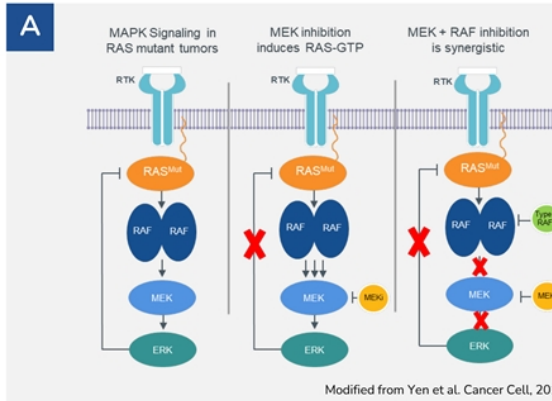
- Pimasertib is an orally-bioavailable, selective, non-competitive MEK1/2 inhibitor in-licensed from Merck KGaA in February 2021
- Extensive non-clinical and clinical development work through Phase 2, including a solid tumor trial in Japan and combinations with other MOAs
- Main AEs typical for all in-class allosteric MEK inhibitors (GI, CPK elevation, skin rash, visual disturbances)
- Nearly three-fold higher CNS penetration than other MEKi inhibitors (trametinib or selumetinib)
- Pimasertib showed monotherapy clinical activity, including an improvement in median PFS versus dacarbazine in NRAS mutant melanoma
- Combination with tovorafenib (DAY101) and other targeted therapies may unlock the full value of pimasertib in advanced solid tumors



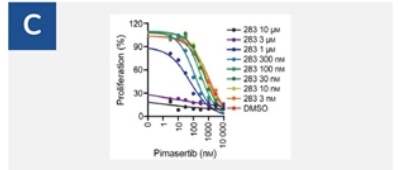
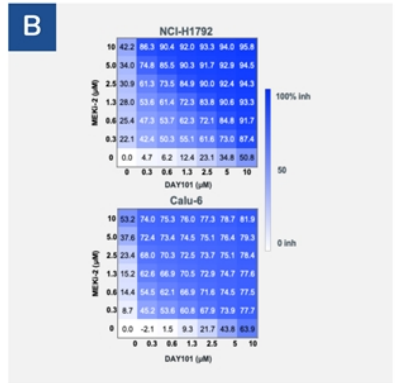
Source: Hepner, Salgues, Anjos, et al. 2017.

Vertical MAPK Pathway Inhibition with Tovorafenib (DAY101) and Pimasertib Unlocks Potential Synergy for Adult Solid Tumors

- The MAPK pathway normally has multiple feedback loops that negatively regulate upstream (RAS/RAF) activation to ensure optimal signaling
- Monotherapy MEK inhibition disables these feedback loops and induces RAS signaling as well as RAF dimerization and activation
- Combination therapy with a MEK inhibitor and type II RAF inhibitor is synergistic in KRASmut and BRAFmut tumor models



- A** Mechanistic model for vertical MAPK pathway inhibition (modified from Yen et al. Cancer Cell, 2018) .
- B** DAY101 + MEK inhibitor is synergistic in KRAS G12C and Q61 mutant tumor cell models (Day One internal data)
- C** Sensitivity of KRAS Q61 mutant cells to pimasertib is enhanced when cells are treated with the type II RAF inhibitor BGB-283 (Yuan et al., Mol Onc 2020)



Tovorafenib (DAY101) / Pimasertib Combination to be Evaluated in Solid Tumors (FIRELIGHT-1)

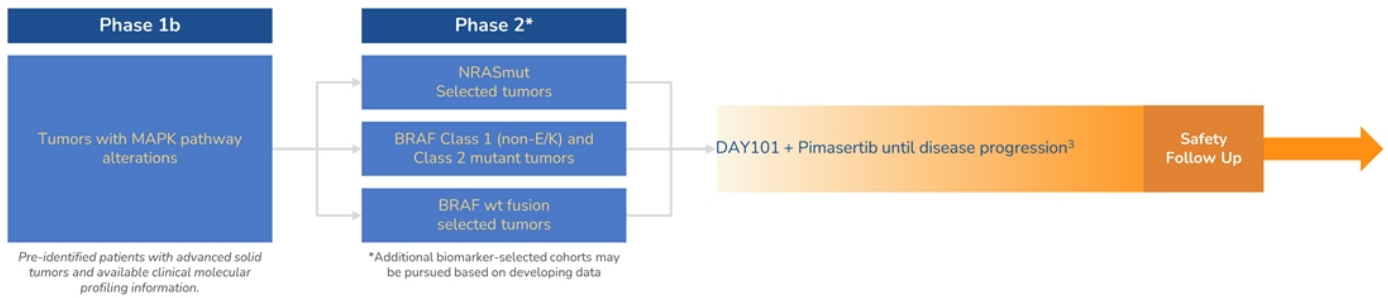


Trial Design¹

- Combination dose escalation, global phase 1b/2 trial²
- Phase 1b, BOIN (adaptive), n = 10/cohort (approximately)
- Phase 2, Simon 2-stage, n = 25/cohort (approximately)
- Eligibility: Patients aged 12 years and older, dose escalation will be performed in advanced solid tumor patients with any MAPK alteration. Expansion cohorts will focus on indications with a potential path to accelerated approval

Endpoints

- Phase 1b: PK, PD and Safety, MTD/RP2D
- Phase 2: Efficacy (ORR, DOR)



Abbreviations: BOIN, Bayesian Optimal Interval Design; BRAF, B-Raf proto-oncogene, serine/threonine kinase; MAPK, mitogen-activated protein kinase; NRAS, neuroblastoma rat sarcoma viral oncogene.
 1. Umbrella master study – DAY101-102 (main protocol) DAY101 and MAPK pathway aberration, Sub-study 1 monotherapy (DAY101-102a), Sub-study 2 MEK combo (DAY101-102b).
 2. Intend to open U.S. and ex-U.S. clinical sites. ³DAY101 + Pimasertib until disease progression, intolerable toxicity, withdrawal of consent, or death

Summary

Financial Summary: DAWN

Cash, cash equivalents and short-term investments as of June 30, 2022: \$394.9 million (no debt)

Follow-on in June 2022: \$172.5 million in gross proceeds, includes full exercise of underwriters' option

73.5 million shares of common stock outstanding as of August 1, 2022

\$ Millions	Six Months Ended 6/30/22	Six Months Ended 6/30/21
R&D Expense	\$37.6	\$22.5
G&A Expense	\$26.9	\$9.0
Net Loss	\$64.3	\$31.6

**Projected
cash runway
into 2025**

FIREFLY-1: Pivotal Phase 2 clinical trial of tovorafenib (DAY101)

- Pivotal cohort enrollment completed in May 2022
- Initial clinical data presented in June 2022
- Full topline results expected in Q1 2023
- NDA submission planned in 1H 2023, if data from FIREFLY-1 is supportive

FIREFLY-2/LOGGIC: Pivotal Phase 3 clinical trial of tovorafenib (DAY101) in newly diagnosed pLGG

- Trial initiated in June 2022
- First patient dosing expected in 2H 2022

FIRELIGHT-1: Tovorafenib (DAY101) and pimasertib combination

- First patient dosed in May 2022

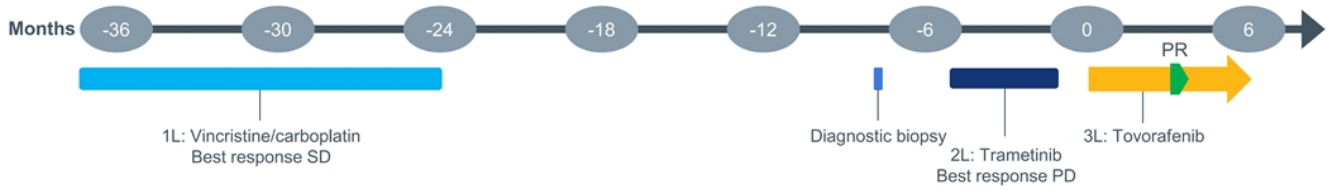
Appendix

Day One Biopharmaceuticals

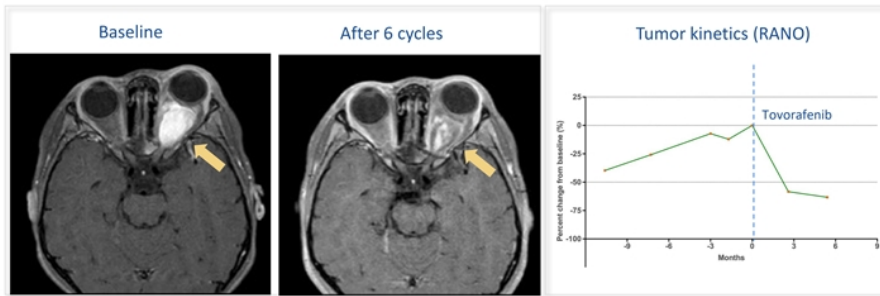


Case Study: Activity Of Tovorafenib (DAY101) In KIAA1549-BRAF Fusion Optic Pathway Glioma

A 7-years-old female child with an optic pathway glioma, with very poor vision, entropion, folliculitis, eczema, mouth ulceration and xerosis



- PR (-58%) and improvement in vision reported at cycle 3
- AEs included grade 3 erythematous rash requiring dose interruption and dose reduction (400 mg QW to 300 mg QW in cycle 1), and grade 2 eczema and maculopapular rash
- Patient continues to receive weekly tovorafenib

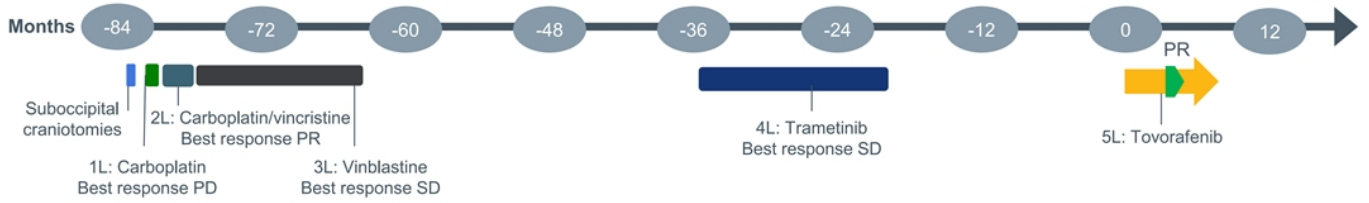


Apr 14, 2022 data cutoff. Tovorafenib is an investigational agent. Safety and efficacy have not been established by any health authority.

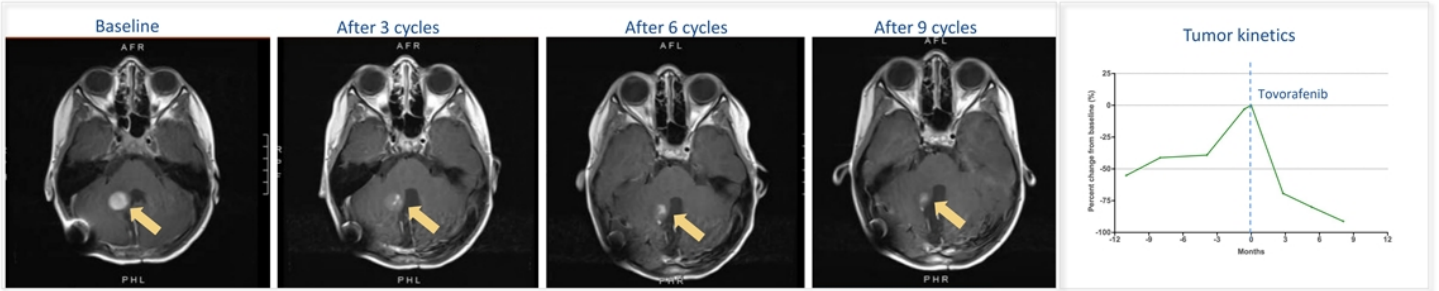
Day One Biopharmaceuticals

Case Study: Activity Of Tovorafenib (DAY101) In KIAA1549-BRAF Fusion Posterior Fossa Pilocytic Astrocytoma

An 8-years-old female child with a posterior fossa pilocytic astrocytoma, eczema, nausea and constipation



- PR (-69%) at cycle 3 with 500 mg QW tovorafenib, with a deepening of response (80% and 91% in cycles 6 and 9, respectively) over time
- AEs included grade 2 decrease in neutrophil count, pustular rash, and upper respiratory infection
- Patient continues to receive weekly tovorafenib



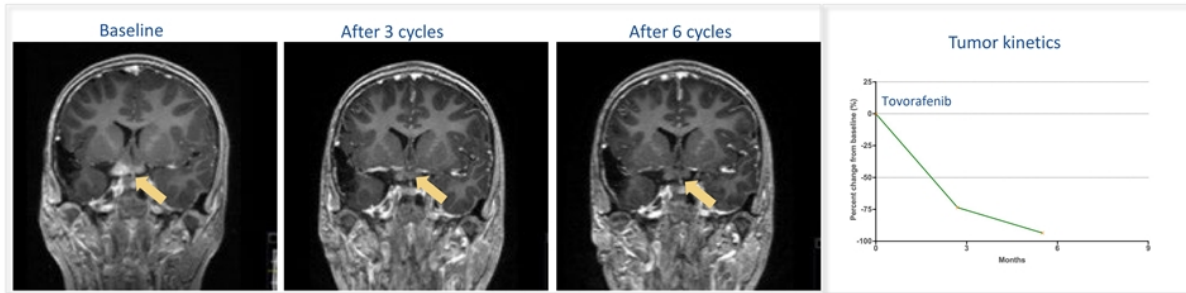
Apr 14, 2022 data cutoff. Tovorafenib is an investigational agent. Safety and efficacy have not been established by any health authority.

Case Study: Activity Of Tovorafenib (DAY101) In BRAF V600E Mutation Deep Midline Astrocytoma

A 9-year-old female child with deep midline BRAF V600E-mutant astrocytoma with precocious puberty



- PR (-74%) at cycle 3, with a deepening of response (-94%) at cycle 6
- AEs included grade 3 maculopapular rash and increased CPK, requiring drug interruption and dose reduction (500 mg QW to 400 mg QW in cycle 1)
- Tovorafenib dose was re-escalated back to 500 mg QW in cycle 4; patient continues on treatment



Apr 14, 2022 data cutoff. Tovorafenib is an investigational agent. Safety and efficacy have not been established by any health authority.

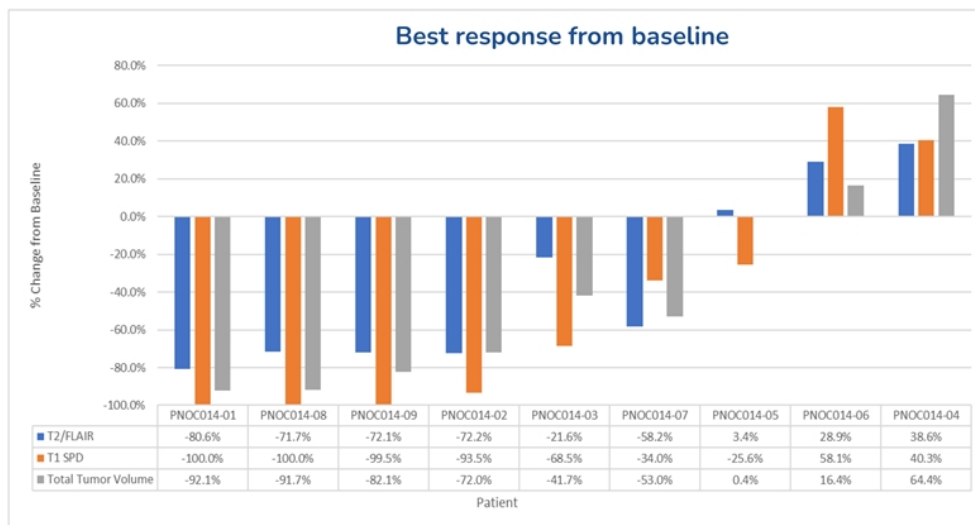
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FIREFLY-1 Study Status

- First patient dosed in May 2021. Registrational pLGG arm completed enrollment in May 2022
- ~35 sites opened across 11 countries
- Expanded access to patients with pLGG (arm 2) and *RAF* fusion-positive solid tumors (arm 3)
- Interim efficacy and safety analysis in the first 25 consecutively enrolled patients who had:
 - Received at least 1 dose of study treatment
 - At least 6 months of follow-up as of April 14, 2022
- Tumor assessments according to RANO criteria, as determined by a blinded independent radiological review committee
- 22 patients with RANO-evaluable tumors

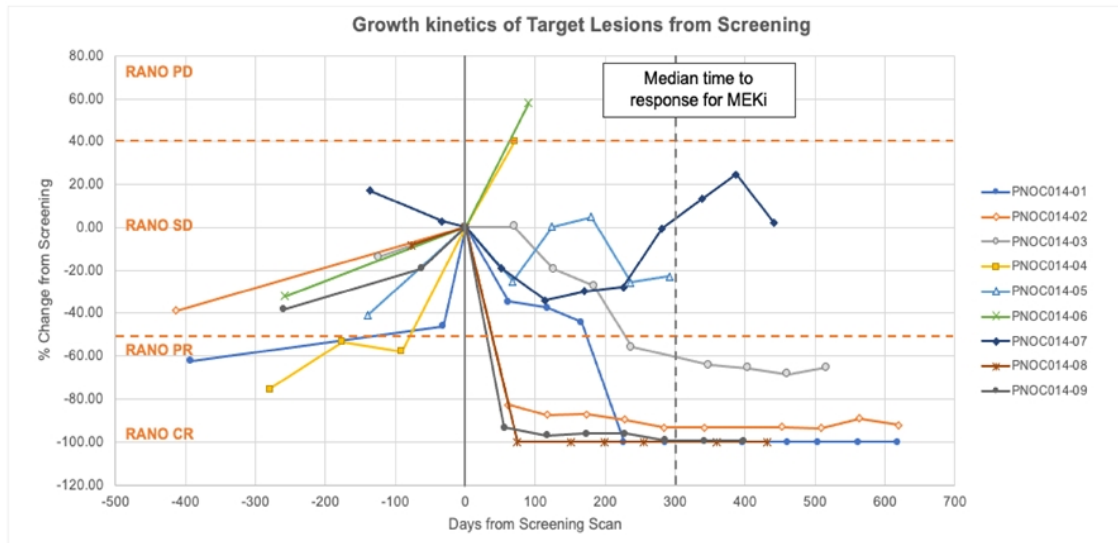


Results from Independent Radiology Review of PNOC014



- RANO: Response assessment for neuro-oncology (FDA standard)
- Volumetric image analysis (exploratory)
- RAPNO: Response assessment for pediatric neuro-oncology (exploratory)

Multiple Rapid, Deep and Durable Responses Observed following Initiation of Tovorafenib (DAY101) Treatment of pLGG Patients in PNOC014



Date of data cutoff: 02 JAN 2020
 Adapted from Wright K et al. Neuro Oncology Abstract CTNI-19. 2020
 Fangusaro J et al. Lancet Oncol 2019

Day One Biopharmaceuticals

Drug-related Adverse Events Observed for Tovorafenib (DAY101) in PNOC014 Showed Favorable Safety and Tolerability Profile in pLGG

DAY101 AE summary

- Most common toxicity: skin
- AEs reversible and all manageable
- Single, reversible Grade 3 event
- No Grade 4 AEs
- No dose reductions (vs. 40% of patients on selumetinib monotherapy required dose reductions)

Drug-related AEs for Tovorafenib (DAY101)

Toxicities	Grade 1-2	Grade 3	Grade 4
Anemia	6 (67%)		
Hypophosphatemia	4 (44%)		
Fatigue	5 (55%)		
Rash	8 (89%)		
Achromotrichia	7 (78%)		
Pruritis	6 (67%)		
Photosensitivity	1 (11%)		
Nevus	7 (78%)		
Alopecia	3 (34%)		
Epistaxis	2 (22%)		
Dry skin	3 (34%)		
Myalgias/artralgias	3 (34%)		
Anorexia	2 (22%)		
Cheilitis	3 (34%)		
Hypermagnesemia	1 (11%)		
Bleeding gums	1 (11%)		
Increased AST	4 (44%)		
Nausea/vomiting	3 (33%)		
CPK elevation		1 (11%)	
Weight loss	2 (22%)		

Drug-related AEs for selumetinib

Toxicities	Grade 1-2	Grade 3	Grade 4
Increased ALT	20 (40%)	1 (2%)	
CPK elevation	34 (68%)	5 (10%)	
Diarrhea	27 (54%)	2 (4%)	
Decreased ejection fraction	19 (38%)	1 (2%)	
Gastric haemorrhage		1 (2%)	
Headache	14 (28%)	1 (2%)	
Decreased lymphocyte count	19 (38%)		1 (2%)
Neutropenia	14 (28%)	3 (6%)	
Paronychia	19 (38%)	3 (6%)	
Rash (acneiform)	29 (58%)	2 (4%)	
Rash (maculopapular)	26 (52%)	5 (10%)	
Skin infection	7 (14%)	1 (2%)	
Tooth infection		1 (2%)	
Weight gain	5 (10%)	1 (2%)	
Vomiting	22 (44%)		
Nausea	21 (42%)		
Increased AST	25 (50%)		
Anemia	28 (56%)		
Pruritis	10 (20%)		
Dyspnea	30 (60%)		